REMARKS

Entry of the above amendments is respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification. The attached pages are captioned **"Version with Markings to Show Changes Made."**

A. Amendments to the Specification

The specification is amended to identify amino and nucleic acid sequences by sequence identification numbers corresponding to the same sequences in the sequence listing. The specification is also amended to correct several misspellings and mistypings.

The amendments to the specification add no new matter.

B. Sequence Listing:

The amended specification now properly identifies amino and nucleic acid sequences by sequence identification numbers which can be found in the sequence listing as originally filed. Accordingly, no new matter has been introduced into the application as a result of the present amendment.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4405.

Respectfully submitted,

Date: 6-30-03

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Version with Markings to Show Changes Made

On page 6, please amend the paragraph starting on line 6 as follows:

As used herein, "OVA" refers to native ovalbumin; "*" refers to the immunodominant OVA-derived peptide SIINFEKL (SEQ ID NO: 22); "HER500" refers to the recombinant fusion human HER-2 protein consisting of one half of its extracellular portion fused to the 1/4 of its intracellular part; "HER500*" refers to the recombinant fusion protein made of HER500 and the immunodominant OVA-derived peptide SIINFEKL (SEQ ID NO: 22) inserted between its extracellular and intracellular components; "HER500*•rGM-CSF" refers to the recombinant fusion protein composed of HER500* and rat granulocyte/macrophage colony-stimulating factor (GM-CSF); "HER500•hGM-CSF" refers to the recombinant fusion protein composed of HER500 and human GM-CSF; and "HER300*•rGM-CSF" refers to the recombinant fusion human HER-2 protein consisting of one half of its extracellular portion fused to the immunodominant OVA-derived peptide SIINFEKL (SEQ ID NO: 22) and rat GM-CSF, as summarized below.

On page 10, please amend the paragraph starting on line 13 as follows:

An immunostimulatory fusion protein construct of the invention may also include one or more sequence components selected from the group consisting of GM-CSF, a reporter sequence such as the [imunodominant]immunodominant OVA-derived octapeptide SIINFEKL ($OVA_{257-264}$, SEQ ID NO: 22), one or more peptide signal sequences and a synthetic purification tag, e.g., an added C-terminal amino acid sequence.

On page 11, please amend the paragraph starting on line 6 as follows:

The immunostimulatory fusion proteins of the invention may be modified by joining them, either covalently or noncovalently, with a reporter molecule. A wide variety of reporter molecules are known in the art and the selection of the reporter determines the assay format. For example, as detailed in Example 1, the OVA-derived [imunodominant]immunodominant octapeptide SIINFEKL ($OVA_{257-264}$, SEQ ID NO: 22) was incorporated into exemplary immunostimulatory HER-2 fusion constructs and antigen presentation of the constructs evaluated. Briefly, the IL-2 secreting mouse T cell hybridoma B3Z, which responds to SIINFEKL ($OVA_{257-264}$, SEQ ID NO: 22), when bound to mouse MHC class I, was stimulated with DC that were pre-pulsed with the HER-2 fusion constructs, and the magnitude of response evaluated by measuring [^{3}H]thymidine incorporation in proliferating IL-2 dependent cells, as an indicator of antigen presentation.

On page 13, please amend the paragraph starting on line 1 as follows:

The exemplary HER500* construct (SEQ ID NO:8) was produced by expression of a coding sequence including in the 5' to 3' direction: the coding sequence for a 32 amino acid PAP signal sequence, the coding sequence for a 3 amino acid sequence of the mature PAP protein, an Ala Arg linker, the coding sequence for a 3 amino acid HER-2 signal sequence, the coding sequence for 289 amino acids of mature HER-2 membrane distal extracellular domain, an Ala linker, the coding sequence for the OVA-derived [imunodominant]immunodominant octapeptide SIINFEKL ($OVA_{257-264}$, SEQ ID NO: 22), the coding sequence for 217 amino acids of the HER-2 membrane distal intracellular domain, three consecutive alanines, and six consecutive histidines.

On page 13, please amend the paragraph starting on line 9 as follows:

The exemplary HER500*•rGM-CSF construct (SEQ ID NO:9) was produced by expression of a coding sequence including in the 5' to 3' direction: the coding sequence for a 32 amino acid PAP signal sequence, the coding sequence for a 3 amino acid sequence of the mature PAP protein, an Ala Arg linker, the coding sequence for a 3 amino acid HER-2 signal sequence, the coding sequence for 289 amino acids of mature HER-2 membrane distal extracellular domain, an Ala linker, the coding sequence for the OVA-derived [imunodominant]immunodominant octapeptide SIINFEKL ($OVA_{257-264}$, SEQ ID NO: 22), the coding sequence for 217 amino acids of the HER-2 membrane distal intracellular domain, an Ala Ala linker, the coding sequence for mature rat GM-CSF (127 residues), and the coding sequence for glycine, alanine, four consecutive prolines, alanine, and six consecutive histidines.

On page 13, please amend the paragraph starting on line 19 as follows:

The exemplary HER300*•rGM-CSF construct (SEQ ID NO:10) was produced by expression of a coding sequence including in the 5' to 3' direction: the coding sequence for a 32 amino acid PAP signal sequence, the coding sequence for a 3 amino acid sequence of the mature PAP protein, an Ala Arg linker, the coding sequence for a 3 amino acid HER-2 signal sequence, the coding sequence for 289 amino acids of mature HER-2 membrane distal extracellular domain, an Ala linker, the coding sequence for the OVA-derived [imunodominant]immunodominant octapeptide SIINFEKL ($OVA_{257-264}$, SEQ ID NO: 22), an Ala linker, the coding sequence for mature rat GM-CSF (127 residues), and the coding sequence for glycine, alanine, four consecutive prolines, alanine, and six consecutive histidines.

On page 23, please amend the paragraph starting on line 25 as follows:

The HER500*•rGM-CSF construct (SEQ ID NO: 4) was produced by expression of a coding sequence which included, in the 5' to 3' direction: a 32 amino acid PAP signal peptide, a 3 amino acid sequence of the mature PAP protein, an Ala Arg linker, a 3 amino acid HER-2 signal sequence, 289 amino acids of the mature HER-2 membrane distal extracellular domain, an Ala linker, the OVA-derived [imunodominant]immunodominant octapeptide SIINFEKL ($OVA_{257-264}$,

SEQ ID NO: 22), 217 amino acids of the HER-2 membrane distal intracellular domain, an Ala Ala linker, a 127 amino acid mature rat GM-CSF sequence, and Gly Ala Pro Pro Pro Pro Ala His His His His His His (SEQ ID NO: 17).

On page 23, please amend the paragraph starting on line 33 as follows:

The HER300*•rGM-CSF construct (SEQ ID NO: 5) was produced by expression of a coding sequence which included, in the 5' to 3' direction: a 32 amino acid PAP signal sequence, a 3 amino acid sequence of the mature PAP protein, an Ala Arg linker, a 3 amino acid HER-2 signal sequence, 289 amino acids of the mature HER-2 membrane distal extracellular domain, an Ala linker, the OVA-derived [imunodominant]immunodominant octapeptide SIINFEKL ($OVA_{257-264}$, SEQ ID NO: 22), an Ala linker, a 127 amino acid mature rat GM-CSF sequence, and Gly Ala Pro Pro Pro Pro Ala His His His His His His (SEQ ID NO: 17).

On page 25, please amend the paragraph starting on line 6 as follows:

The HER500 construct (SEQ ID NO: 1) was produced by expression of a coding sequence which included, in the 5' to 3' direction: a 32 amino acid PAP signal sequence, a 3 amino acid sequence of the mature PAP protein, an Ala Arg linker, 3 amino acids of HER-2 signal sequence, 289 amino acids of mature HER-2 membrane distal extracellular domain, 217 amino acids of the HER-2 membrane distal intracellular domain and a C-terminal tag consisting of Ala Ala Ala His His His His His His (SEQ ID NO: 15).

On page 25, please amend the paragraph starting on line 12 as follows:

The HER500•hGM-CSF construct (SEQ ID NO: 2) was produced by expression of a coding sequence which included, in the 5' to 3' direction: a 32 amino acid PAP signal sequence, a 3 amino acid sequence of the mature PAP protein, an Ala Arg linker, 3 amino acids of HER-2 signal sequence, 289 amino acids of the mature HER-2 membrane distal extracellular domain, 217 amino acids of the HER-2 membrane intracellular domain, an Ala Ala linker, a 127 amino acid mature human GM-CSF sequence and a C-terminal tag consisting of Gly Ala Pro Pro Pro Pro Ala Ala Ala His His His His His His (SEQ ID NO: 16).

On page 25, please amend the paragraph starting on line 19 as follows:

The HER500* construct (SEQ ID NO: 3) was produced by expression of a coding sequence which included, in the 5' to 3' direction: [the coding sequence for:]a 32 amino acid PAP signal sequence, a 3 amino acid sequence of the mature PAP protein, an Ala Arg linker, 3 amino acids of HER-2 signal sequence, 289 amino acids of the mature HER-2 membrane distal extracellular domain, an Ala linker, the OVA-derived [imunodominant]immunodominant octapeptide SIINFEKL ($OVA_{257-264}$, SEQ ID NO: 22), 217 amino acids of the HER2 membrane

distal intracellular domain and a C-terminal tag consisting of Ala Ala Ala His His His His His His (SEQ ID NO: 15).

On page 25, please amend the paragraph starting on line 26 as follows:

The HER500*rGM-CSF construct (SEQ ID NO: 4) was produced by expression of a coding sequence which included, in the 5' to 3' direction: a 32 amino acid PAP signal sequence, a 3 amino acid sequence of the mature PAP protein, an Ala Arg linker, 3 amino acids of HER-2 signal sequence, 289 amino acids of the mature HER-2 membrane distal extracellular domain, an Ala linker, the OVA-derived [imunodominant]immunodominant octapeptide SIINFEKL ($OVA_{257-264}$, SEQ ID NO: 22), 217 amino acids of the HER2 membrane distal intracellular domain, an Ala Ala linker, a 127 amino acid mature rat GM-CSF sequence and a C-terminal tag consisting of Gly Ala Pro Pro Pro Pro [Pro]Ala His His His His His His (SEQ ID NO: 17).

On page 25, please amend the paragraph starting on line 34 as follows:

The HER300*rGM-CSF construct (SEQ ID NO: 5) was produced by expression of a coding sequence which included, in the 5' to 3' direction: a 32 amino acid PAP signal sequence, a 3 amino acid sequence of the mature PAP protein, an Ala Arg linker, 3 amino acids of HER-2 signal sequence, 289 amino acids of the mature HER-2 membrane distal extracellular domain, an Ala linker, the OVA-derived [imunodominant]immunodominant octapeptide SIINFEKL ($OVA_{257-264}$, SEQ ID NO: 22), an Ala linker, a 127 amino acid mature rat GM-CSF sequence and a C-terminal tag consisting of Gly Ala Pro Pro Pro Pro [Pro]Ala His His His His His His (SEQ ID NO: 17).

On page 31, please amend the third row of the left column as follows:
Reporter peptide in constructs HER500* and HER500*ratGM-CSF: (OVA-derived [imunodominant]immunodominant octapeptide SIINFEKL ($OVA_{257-264}$))